REMARKS

Claims 29-32, 60, 61, 99-136, 138-151 will be pending upon entry of this amendment. Claim 137 has been canceled without prejudice in response to a restriction requirement as it is directed to a non-elected invention. Applicants reserve the right to prosecute the subject matter of this claim in a related application. Claims 29, 30, 60, 61, 99, 105, 107, 108, 109, 110, 113, 114, 128, 129, 131-136 and 138-142 have been amended to clarify the claimed invention. New claims 146-151 have been added.

In particular, claims 29, 30, 60, 61, 107, 108, 109, 113, 114, 129 and 131-136 have been amended that the first nucleic acid hybridizes under high stringency conditions to the second nucleic acid, said high stringency conditions comprising pretreatment for 8 hours to overnight in a solution containing 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 48 hours at 68°C in a solution containing 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 100 µg/ml denatured salmon sperm DNA; washing for 1 hour at 37°C in a solution containing 2X SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA; and a second washing for 45 minutes at 50°C in a solution containing 0.1X SSC. Support for this amendment is found in the specification as filed on page 15, lines 4-20.

Because claim 29 is directed to an antibody and claims 60 and 61 are directed to a composition, claim 99 has been amended and claim 146 has been added to ensure proper antecedent basis for claims 99 and 146. Further, claims 99, 105, 110, 128 have been amended to reflect that SEQ ID NOS:65-80 are separate sequences (although each a part of the complete human Delta sequence). Further, claim 99 has been amended to clarify that, in one alternative in the Markush group, all of SEQ ID NOS:65-80 are present in the vertebrate Delta protein. Support for this amendment is found, *inter alia*, in Figure 14.

Support for newly added claims 147-151 is found in the specification as filed,

inter alia, at page 26, lines 17-24; page 78, lines 19-22; and Figure 11.

No new matter is added by these amendments to the claims.

Applicants note that a Revocation and Power of Attorney, executed on behalf of co-assignee Imperial Cancer Research Trust, Ltd. is submitted herewith appointing those listed under Customer Number 20583 as their representatives to prosecute the above-identified application and transact all business at the U.S. Patent and Trademark Office in connection therewith. A Revocation and Power of Attorney executed on behalf of co-assignee Yale University is intended to be submitted shortly under separate cover.

1. Election/Restrictions

Applicants note that the Examiner states on page 2 of the Office Action that Applicants elected Group I with traverse and based that traversal on the grounds that there are generic claims. Applicants wish to make clear that no traversal was made, much less on the grounds that there are generic claims. Applicants indeed elected Group I, drawn to an antibody, composition comprising the antibody, and method of making the antibody, and elected the species of SEQ ID NO:65 from SEQ ID NOS:65-80. Applicants note that the claims are directed to antibodies to vertebrate Delta proteins and fragments and related molecules and compositions, or to methods of making such antibodies. The claims are not directed to the particular nucleic acids encoding such proteins and fragments. Thus, as set forth in the response filed September 25, 2003, claims 29-32, 60, 61, 100-104, 107-109, 113, 114, 116-118, 121-125, 129-138 and 142-145 are believed to be generic since claims directed to the species of (an antibody to) SEQ ID NO:65 contains all the limitations of a generic claim directed to an antibody to a vertebrate Delta protein, as SEQ ID NO:65 is human Delta sequence.

Further, with regard to the Examiner's reasoning that no reading frame is specified, Applicants note that the claims require that the hybridizable nucleic acid encodes a

vertebrate Delta protein or fragment, which necessarily specifies a reading frame. Thus, claims such as claim 29 recite a proper Markush group.

2. Specification

The specification has been objected to because of a number of alleged errors in the sequence identifiers cited in the specification. Applicants note that in the Preliminary Amendment filed on February 15, 2001, the specification was amended to correct the sequence identifiers recited therein. Applicants are unaware of any errors in the sequence identifiers that were not corrected in the Preliminary Amendment filed February 15, 2001.

3. Claim Objections

Claims 114 and 129 are objected to because of the informality of "is comprises". In response, claims 114 and 129 have been amended to delete "is" before "comprises", thus obviating the reason for the objection.

4. Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 32, 60, 61, 104 and dependent claims 99, 100 and 102 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite for the various reasons set forth below.

Claim 61 is allegedly indefinite for use of the term "derivative". Applicants disagree with the Examiner's allegation; however, in order to advance the prosecution of the present application, Applicants have deleted the term "or derivative" from claim 61, thus obviating the rejection.

Claims 32 and 104 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for using the term "molecule". Applicants respectfully disagree and point out that the second paragraph of Section 112 requires that the claims set out and circumscribe

the particular area which the patent applicant regards as his/her invention with a reasonable degree of precision and particularity. *In re Moore*, 169 U.S.P.Q. 236 (C.C.P.A. 1971). "[A]cceptability depends on 'whether one of ordinary skill in the art would understand what is claimed . . . in light of the specification,' even if experimentation may be needed." *Andrew Corp. v. Gabriel Electronics, Inc.*, 6 U.S.P.Q.2d 2010, 2013 (Fed. Cir. 1988) (citing *Seattle Box Co. v. Industrial Crating & Packing*, 221 U.S.P.Q. 568, 574 (Fed. Cir. 1984)), *cert. denied*, 488 U.S. 927 (1988). Moreover, under the applicable case law, Applicants are entitled to claim their invention in different ways, a reasonable number of times, provided the invention is not obscured by undue multiplicity. *See, In re Barnett*, 69 U.S.P.Q. 609 (C.C.P.A. 1946). Applicants respectfully submit that the term "molecule" in claims 32 and 104 fully meets the requirements of Section 112, second paragraph.

Applicants submit that the term "molecule" is well known in the art and that one skilled in the art can clearly understand what is covered by this claim in light of the specification. A "molecule" is intended to encompass a chemical structure that is not limited, for example, to antibodies. Thus, for example, claim 32 encompasses situations where a fragment of a monoclonal antibody to a vertebrate Delta protein is covalently (*e.g.*, cross-linked) or noncovalently bound to a non-protein moiety.

According to the Examiner, the term molecule not a common phrase in the art and no clarification could be found in the specification. Applicants again disagree with the Examiner and point out that it is well settled law that when a term is not defined in the specification, the term is to be given its ordinary meaning, which ordinary meaning can be found in a dictionary.

> Absent . . . a definition [in the patent] or evidence that the claim limitation as a whole has a special meaning to one of skill in the art, we see no error in the district court's use of dictionary definitions to ascertain the ordinary meaning of the relevant claim limitation. *Quantum Corp. v. Rodime, Plc.* 65 F.3d 1577, 1581, 36 U.S.P.Q.2d 1162, 1166 (Fed. Cir. 1995).

Accordingly, Applicants submit herewith, as Exhibit A, page 1455 of

Webster's Third New International Dictionary of the English Language, G. & C. Merriam Co., pub., 1981 ("Webster's"), which recites the ordinary meaning of "molecule".

According to Webster's, a molecule is defined as:

> 1a: a unit of matter that is the smallest particle of an element or chemical combination of atoms (as a compound) capable of retaining chemical identity with the substance in mass . . .

The term molecule certainly has an art-accepted meaning that is clearly understood by those of skill in the art such that the skilled artisan can clearly interpret the meaning of a claim containing the term "molecule". Accordingly, Applicants respectfully request withdrawal of this Section 112 rejection.

Claims 60 and 61 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for reciting "an amount" of an antibody or fragment. In response, Applicants have amended claims 60 and 61 to delete "an amount of" which obviates the rejection.

In view of the foregoing amendments and arguments, Applicants respectfully submit that the rejections under 35 U.S.C. § 112, second paragraph, have been obviated or overcome. Therefore, Applicants respectfully request their withdrawal.

5. Rejections under 35 U.S.C. § 103(a)

A. Claims 109, 110, 113, 114, 116-118, 121-126, 128-136, 138, 139 and 142-145 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Lindsell et al., 1995, Cell 80(6):909-917 ("Lindsell") or Henrique et al., 1995, Nature 375:736-737 ("Henrique") in view of U.S. Patent No. 5,648,464 ("the '464 patent"). According to the Examiner, "[i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to use the methods of U.S. Patent No. 5,648,464 to make antibodies, including purified antibodies for use in assays, to the Jagged ligand taught by Lindsell et al." Applicants respectfully disagree.

Preliminarily, Applicants note that the claims have been amended to recite that the first nucleic acid which encodes a vertebrate Delta protein hybridizes under high stringency conditions to the second nucleic acid, said high stringency conditions comprising pretreatment for 8 hours to overnight in a solution containing 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 µg/ml denatured salmon sperm DNA; hybridization for 48 hours at 68°C in a solution containing 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 100 µg/ml denatured salmon sperm DNA; washing for 1 hour at 37°C in a solution containing 2X SSC, 0.01% PVP, 0.01% Ficoll, and 0.01% BSA; and a second washing for 45 minutes at 50°C in a solution containing 0.1X SSC.

Further, Applicants respectfully point out that Henrique is not prior art since it is not a publication by another and was published less than one year before the effective filing date of the claimed invention. The present application is a divisional of U.S. Application No. 08/981,392 filed April 7, 1998, now U.S. Patent No. 6,262,025, which is a national stage application under 35 U.S.C. § 371 of International Application No. PCT/US96/11178 filed June 28, 1996, which claims priority to U.S. Provisional Application No. 60/000,589 filed June 28, 1995. The volume in which Henrique appears is dated June 29, 1995. Thus, even assuming *arguendo* that the claims were not supported under 35 U.S.C. § 112 in the provisional application (which is not conceded to be the case), Henrique is not a publication of another, since Henrique is not prior art under Section 102(a) for reasons described below.

35 U.S.C. § 102(a) requires that

> the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent[.]

Henrique is co-authored by co-inventors Domingos M.P. Henrique, Julian H. Lewis and David Ish-Horowicz, and others, and was published on June 29, 1995, which is prior to the provisional application filing date and within one year of the filing date of the

International application, which is the latest effective filing date of the present application, *i.e.*, June 28, 1996. Thus, regardless whether the claimed invention is supported in the provisional application or in the International application, Applicants therefore contend that Henrique is not available as prior art for any purpose under 35 U.S.C. § 102 or § 103. To support this contention, Applicants provide the accompanying Declaration of Drs. Domingos M.P. Henrique, Julian H. Lewis, David Ish-Horowicz, Spyridon Artavanis-Tsakonas, and Grace E. Gray Under 37 C.F.R. § 1.132 ("Declaration") as evidence that Henrique is the inventors' own publication, which occurred less than one year prior to the filing date of the International application. *In re Katz*, 687 F.2d 450, 215 U.S.P.Q. 14 (C.C.P.A. 1982). In view of the facts set forth in the Declaration by the inventors, Applicants submit that Henrique cannot be used in this or any other rejection under 35 U.S.C. § 102(a) or § 103(a).

Lindsell discloses rat Jagged nucleotide and amino acid sequences, but does not teach or suggest antibodies to rat Jagged, much less antibodies to a vertebrate Delta protein or methods for making antibodies to a vertebrate Delta protein. Applicants note that Jagged is not a vertebrate Delta protein and that nucleic acids encoding Jagged would not be expected to hybridize under high stringency conditions to nucleic acids encoding vertebrate Delta. According to Lindsell on page 910, left column, Jagged is a ligand for rat Notch and is closely related to Serrate[1], which is distinct from vertebrate Delta. The '464 patent discloses nucleotide and amino acid sequences of human Notch and *Drosophila* Delta, as well as methods for making antibodies thereto. The '464 patent does not disclose or suggest any vertebrate Delta nucleotide or amino acid sequences or sequences that would hybridize thereto under high stringency conditions.

For a rejection under Section 103(a) for obviousness to be upheld, the prior art must have suggested to those of ordinary skill in the art that they should make the claimed

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[1] *See, also*, Henrique at page 790, left column, which states that Jagged is a Serrate-related gene that appears to be the rat homologue of the chick Serrate gene.

composition or device or use the claimed method, as the case may be; and the prior art must have revealed that in so doing, those of ordinary skill would have had a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991); *In re Dow Chemical Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). There is nothing in the cited references, alone or in combination, that suggests to one skilled in the art the claimed methods for making antibodies that bind to a vertebrate Delta protein, nor do the cited references provide a reasonable expectation of success in obtaining such antibodies. The disclosure of rat Jagged sequences and a method for antibody production simply does not provide a suggestion of an antibody to a vertebrate Delta protein. Additionally, there is no reasonable expectation of success in obtaining an antibody that binds to a vertebrate Delta protein, since the skilled artisan would not reasonably expect to generate antibodies to a vertebrate Delta protein using a Jagged protein.

With respect to the Examiner's speculation that antibodies against the Jagged protein of Lindsell could be reactive with SEQ ID NO:65 (human Delta sequence), Applicants respectfully submit that the Examiner is improperly using an inherency analysis. First, Applicants point out that the Examiner has not provided any evidence or reasonable basis for the Examiner's speculative assertion. Further, to the extent that the Examiner is arguing that antibodies to Jagged would inherently bind to (crossreact with) SEQ ID NO:65, the basis for the rejection is improper. Applicants point out that such crossreactivity is not an "inherent" property of anti-Jagged antibodies since the skilled artisan would not have appreciated or recognized that antibodies that crossreact with vertebrate Delta could have been obtained using Jagged sequences. Inherency is immaterial in an obviousness analysis if the record establishes that one of ordinary skill would not appreciate the inherent feature. *In re Shetty*, 566 F.2d 81, 195 U.S.P.Q. 753 (C.C.P.A. 1977). As stated by the CCPA in *In re Spormann*, "[t]hat which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." *In re Spormann*, 363 F.2d 444, 448, 150 U.S.P.Q. 449, 452

(C.C.P.A. 1966); *see also W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1555, 220 U.S.P.Q. 303, 314-15 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

Further, Applicants point out that even assuming *arguendo* that inherency were applicable (which it is not), the references cited by the Examiner fail to give rise to a case of inherent anticipation since inherency requires that all the elements of the claim must necessarily, inevitably, and always result from the prior art disclosure and would be so recognized by one of ordinary skill in the art; mere possibilities or probabilities are not sufficient. *See Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1269, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991); *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1553-54, 220 U.S.P.Q. 303, 313-14 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984); *In re Oelrich*, 666 F.2d 578, 581, 212 U.S.P.Q. 323, 325-26 (C.C.P.A. 1981). The Examiner has presented no evidence that using the Jagged protein disclosed by Lindsell (or the proteins disclosed in the '464 patent) as an immunogen would necessarily, inevitably, and always result in an antibody that crossreacts with a vertebrate Delta protein. The Examiner's speculation that antibodies that crossreact with vertebrate Delta may result by using the Jagged protein taught by Lindsell is not legally sufficient to establish inherent anticipation, much less obviousness.

With regard to the Examiner's unsupported allegation that the chick and rat sequences would be identified by low stringency hybridization to the vertebrate Delta sequences of the invention, Applicants note that the claims now specify that the hybridization conditions are of high stringency. It is believed that the rat Jagged sequence does not hybridize to the Delta sequences recited in the claims under such high stringency conditions. The chick sequences of Henrique are not prior art, as discussed above. Further, Applicants point out that even assuming *arguendo* that the allegation were correct, such does not provide a proper basis for the Examiner's rejection. The claims specify methods for making an antibody to a vertebrate Delta protein. As discussed above, the proteins of Lindsell or the

'464 patent are not vertebrate Delta proteins.

Thus, the Examiner's rejection is erroneous and Applicants respectfully request its withdrawal.

B. Claims 29-32, 60, 61, 99-105, 107 and 108 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Henrique et al., 1995, Nature 375:736-737 ("Henrique"), in view of International Patent Publication WO 92/19734 ("International Publication").

As discussed above, Henrique cannot be used as a prior art reference since it is not art under 35 U.S.C. § 102. The International Publication, which claims priority to the application which matured as U.S. Patent No. 5,648,464 discussed above, discloses human Notch, and *Drosophila* Delta and *Drosophila* Serrate sequences as well as methods for producing antibodies to such sequences. The International Publication does not teach vertebrate Delta sequences, much less antibodies to such sequences, and, thus, the International Publication does not render obvious claims directed to vertebrate Delta antibodies and does not provide a reasonable expectation of success in obtaining vertebrate Delta sequences based on its disclosure of *Drosophila* Delta sequences. *Cf., In re Deuel*, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995).

For a rejection of claimed subject matter as obvious in view of a combination of prior art references to be upheld, (1) the prior art must have suggested to those of ordinary skill in the art that they should make the claimed composition or device or use the claimed method, as the case may be; and (2) the prior art must have revealed that in so doing, those of ordinary skill would have had a reasonable expectation of success. *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991); *In re O'Farrell*, 7 U.S.P.Q.2d 1673 (Fed. Cir. 1988); *In re Dow Chemical Co.*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). The International Publication does not suggest the claimed antibodies to vertebrate Delta proteins, much less provide a reasonable expectation of success in obtaining the antibodies since the International Publication does not suggest vertebrate Delta sequences.

In view of the foregoing discussion, Applicants submit that this Section 103 rejection has been overcome and respectfully request its withdrawal.

CONCLUSION

Applicants respectfully request that the above-made remarks of the present response be entered and made of record in the file history present application.

Applicants request that the Examiner call Adriane M. Antler at (212) 326-3630 if any questions or issues remain.

Respectfully submitted,

Date: September 9, 2004

Adriane M. Antler — 32,605 (Reg. No.)

By: William Thomann — 40,203 (Reg. No.)

JONES DAY
222 East 41st Street
New York, New York 10017-6702
(212) 901-9028

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esp : GRAM MOLECULE ⟨a ~ of any substance contains the same number of molecules —Farrington Daniels & R.A.Alberty⟩

²mo·le \'mō(ˌ)lā\ *n, usu cap* : MOSSI

³mo·le \'mōlē\ *n* -s [MexSp, fr. Nahuatl *mulli, molli* sauce, stew] : a highly spiced sauce made principally of chile and chocolate but containing numerous other ingredients and served with meat (as beef or turkey)

molecast \'ˌ=ˌ=\ *n* [³*mole* + *cast*] : MOLEHILL

mole catcher *n* : one that catches moles; *specif* : BROWN KING SNAKE

mole crab *n* : BAIT BUG

mole cricket *n* : an insect of the widespread family Gryllotalpidae (order Orthoptera) having large fossorial front legs adapted for digging in moist soil and feeding largely on the roots of plants

mo·lec·u·la \mə'lekyələ\ *n, pl* **molecu·lae** \-yəˌlē\ [NL — more at MOLECULE] *archaic* : MOLECULE

mo·lec·u·lar \mə'lekyələ(r)\ *adj* [ISV *molecule* + *-ar*] **1** : relating to, connected with, produced by, or consisting of molecules : MOLAR, MOLAL ⟨~ structure⟩ ⟨~ rearrangement⟩ ⟨~ oxygen⟩ **2** : consisting of two or more atomic statements related by logical connectives ⟨~ proposition⟩ — see ¹ATOMIC 4 **3** : relating to or emphasizing individual responses or structures of behavior ⟨proceed by more and more detailed analysis to the ~ facts of perception —G.A.Miller⟩ — opposed to *molar* — **mo·lec·u·lar·ly** *adv*

molecular beam *n* : a stream of molecules that escape at thermal speeds from a heated enclosure, that are controlled by slits so as to move in nearly parallel paths, and that are used in determining the electric and magnetic properties of atoms, atomic nuclei, and molecules

molecular biology *n* : a branch of biology dealing with the ultimate physicochemical organization of living matter

molecular compound *n* : a compound regarded as a union of molecules retaining their identities (as in boron trifluoride-ethyl ether $BF_3.(C_2H_5)_2O$) — called also *addition compound*; compare DOUBLE SALT 2

molecular distillation *n* : distillation that is carried out under a high vacuum in an apparatus so designed as to permit molecules escaping from the warm liquid to reach the cooled surface of the condenser before colliding with other molecules and consequently returning to the liquid and that is used in the purification of substances of low volatility (as in the separation of vitamin A and vitamin E from fish-liver oils)

molecular film *n* : a monomolecular film or layer : MONOLAYER

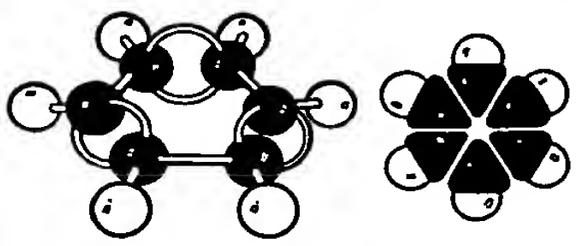
molecular formula *n* : a chemical formula based on both analysis and molecular weight ⟨$C_2H_4O_2$ and $C_6H_{12}O_6$ are the *molecular formulas* of acetic acid and glucose respectively or twice and six times the empirical formulas respectively⟩ — compare STRUCTURAL FORMULA

molecular heat *n* : the heat capacity per gram molecule of any pure substance : the specific heat in calories per degree per gram multiplied by the molecular weight — compare ATOMIC HEAT

mo·lec·u·lar·i·ty \məˌlekyə'larəd·ē *also* -'ler-\ *n* -ES : the quality, state, or degree of being molecular; *esp* : the number of molecules or atoms involved in a chemical reaction ⟨there is no necessary correlation between the ~ and the order — Farrington Daniels & R.A.Alberty⟩

molecular layer *n* **1** : the outer layer of the cortex of the cerebellum and cerebrum consisting of a mass of unmedullated fibers rich in synapses **2** : either of the two plexiform layers of the retina

molecular model *n* : a scale model showing the arrangement of



two molecular models of benzene, in which carbon atoms are represented by dark balls and quasi tetrahedrons, and hydrogen atoms by light balls and half spheres

atoms in a molecule (as of an organic compound)

molecular pump *n* : a vacuum pump that depends for its action on the adhesion of the gas or vapor molecules to a rapidly moving metal disk or cylinder by which they are carried away

molecular rotation *n* : a value obtained by multiplying the specific rotation by the molecular weight

molecular sieve *n* : a crystalline substance (as a zeolite) that is characterized by pores of molecular dimensions and uniform size formed by heating to drive off the water of hydration and that by its ability to adsorb small molecules but not large ones can be used esp. in separations (as of gases or liquids) based on differences in sizes of molecules or as a carrier (as of accelerators in rubber vulcanization)

molecular silver *n* : a gray powdery active form of silver obtained by reducing silver chloride with zinc

molecular spectrum *n* : a spectrum of radiation due to electron transitions and other quantum energy changes within molecules and consisting of series of characteristic spectrum bands which are found upon high dispersion to be made up of very fine lines

molecular still *n* : an apparatus for carrying out a molecular distillation

molecular volume *n* : the quotient obtained by dividing the molecular weight by the specific gravity — compare ATOMIC VOLUME

molecular weight *n* : the weight of a molecule that may be calculated as the sum of the atomic weights of its constituent atoms

mol·e·cule \'mälˌkyül, -lē,-\ *n* -S [F *molécule*, fr. NL *molecula*, dim. of L *moles* mass — more at MOLE (structure)] **1 a** : a unit of matter that is the smallest particle of an element or chemical combination of atoms (as a compound) capable of retaining chemical identity with the substance in mass ⟨a few elements (as helium and neon) have monatomic ~s⟩ ⟨the viruses are one kind of giant ~s —Linus Pauling⟩ — see AVOGADRO'S LAW; compare ION, RADICAL 5 **b** : a quantity proportional to the molecular weight; *esp* : ⁷MOLE **2** : a tiny bit : FRACTION, FRAGMENT ⟨every tone . . . is a ~ of music — Henry Miller⟩ ⟨a ~ of political honesty —*Time*⟩

moled *past of* MOLE

mole drain *n* [³*mole*] : an underground channel made by a mole plow and used esp. for draining heavy farm soils of more or less uniform slope

mole drainage *or* **mole draining** *n* : an act, instance, or system of drawing off water from farmland by mole drains

mole fraction *n* [⁷*mole*] : the ratio of the number of moles of one component of a solution or other mixture to the total number of moles representing all of the components

mole gray *n* : ³MOLE 4

molehill \'ˌ=ˌ=\ *n* [ME, fr. *mole* + *hill*] **1** : a little ridge of earth thrown up by a mole working close to the surface — called also *molecast* **2** : an insignificant obstacle or difficulty : TRIFLE ⟨make a mountain out of a ~⟩

mole mouse *n* : SOKHOR

mole plant *also* **mole tree** *n* : CAPER SPURGE

mole plow *or* **mole drainer** *n* [³*mole*] : a subsoil plow having a vertical knife behind the tooth of which is drawn a round or tapered metal ball that opens an underground channel

mole rat *n* : any of various rodents resembling true moles in habit or appearance: as **a** : SOKHOR **b** : a member of the family Spalacidae of the eastern Mediterranean region **c** : a member of the family Bathyergidae and esp. of the African genus *Bathyergus* **d** : a member of the East Indian murid genus *Nesokia*

moles *pl of* MOLE, *pres 3d sing. of* MOLE

mole shrew *n* **1 a** : an American short-tailed shrew of the genus *Blarina* **b** : any of several shrews of the genus *Anourosorex* that resemble moles, have the ears and eyes greatly reduced, have slate-colored glossy fur, and live in the high mountains of Burma, China, and Siam **2** : SHREW MOLE

moleskin \'ˌ=ˌ=\ *n* **1** : ³MOLE 1d **2 a** : a heavy durable cotton fabric made in satin weave for industrial, medical, and clothing uses and usu. with a smooth twilled surface on one side and a short thick velvety nap on the other **b** : a garment (as trousers) made of moleskin — usu. used in pl. ⟨got on their boots and ~s —Mary S. Broome⟩ **3** : ³MOLE 4a

mole snake *n* **1** : a valuable colubrid snake (*Pseudaspis cana*) that is common in South and East Africa and feeds on rats and mice **2** : BROWN KING SNAKE

¹mo·lest \mə'lest\ *vt* -ED/-ING/-S [ME *molesten*, fr. MF *molester*, fr. L *molestare*, fr. *molestus* burdensome, annoying, irreg. fr. *moles* mass — more at MOLE (structure)] **1** *obs* **a** : INCONVENIENCE, HARASS, PLAGUE ⟨the heats of summer are . . . incapable of *~ing* you —Joseph Addison⟩ **b** : to affect injuriously : AFFLICT ⟨they were generally *~ed* with . . . sciatica —Sir Thomas Browne⟩ **2 a** : ANNOY, PERSECUTE, DISTURB, TORMENT ⟨painted in a loft, drawing up the ladder after him that he might not be *~ed* by his family —Laurence Binyon⟩ ⟨leaders . . . should not be *~ed* in any way nor should their party be outlawed —Sidney Hook⟩; *specif* : RAID ⟨traders turn to *~ing* the Spanish borderlands —R.A.Billington⟩ **b** : to meddle or interfere with unjustifiably often as a result of abnormal sexual motivation ⟨charges of being drunk and *~ing* a woman —Frank Yerby⟩ ⟨*~ing* small boys in the washroom of a moving picture house —Wenzell Brown⟩

²molest \"\ *n* -S [ME, fr. MF *moleste*, irreg. fr. L *molestia* trouble, fr. *molestus* + *-ia* -y] : MOLESTATION ⟨within his walls, secure from all ~ —W.J.Linton⟩

mo·les·ta·tion \ˌmōˌle'stāshən, -ləˈ-\ *n* -S [ME *molestacioun*, fr. MF *molestation*, fr. LL *molestation-*, *molestatio*, fr. L *molestatus* (past part. of *molestare*) + *-ion-*, *-io* -ion] **1 a** *archaic* : a cause or state of harassment : VEXATION ⟨all the ~s of marriage are abundantly recompensed with other comforts —Thomas Fuller⟩ **b** : an act or instance of molesting : ANNOYANCE, OBSTRUCTION ⟨liberty to . . . worship without ~ — William Sewel⟩ ⟨seas upon which our ships and planes can travel without ~ —*U.S.Code*⟩ **2 a** *Scots law* : interference with or troubling another in his possession of land **b** : willful injury inflicted upon another by interference with his user of rights as to person, character, social position, or property

mo·lest·er \mə'lestə(r)\ *n* -S : one that molests

mo·lest·ful \-tfəl\ *adj, archaic* : TROUBLESOME, ANNOYING ⟨~ battle with carnal vices —Thomas Wright⟩

molet *var of* MULLET

mo·le·ta \mə'lādə\ *n* -S [Pg *moleta, muleta*, fr. *muleta* crutch, fr. Sp — more at MULETA] : a short-masted Portuguese fishing boat having a large lateen sail, two outriggers and a bowsprit that carry up to six sails, and an outrigger at the stern with two triangular sails

moleta

mole·warp \'mōlˌwȯrp\ *var of* MOLDWARP

mol·ge \'mōljē\ [NL, fr. G *molch* salamander, fr. OHG *mol, molm, molt;* akin to OS & MLG *mol* salamander, and perh. to Arm *molēz* lizard] *syn of* TRITURUS

mol·gu·la \'mälgyələ\ *n, cap* [NL, fr. Gk *molgos* hide, skin + NL *-ula;* perh. akin to OHG *malaha* leather bag, ON *malr* bag] : a cosmopolitan genus (the type of the family Molgulidae) of almost spherical ascidians with long siphons and a thin somewhat transparent tunic — **mol·gu·lid** \-ləd\ *adj or n*

¹mo·lid \'mōləd\ *adj* [NL *Molidae*] : of or relating to the Molidae

²molid \"\ *n* -S : a fish of the family Molidae

mol·i·dae \'mäləˌdē\ *n pl, cap* [NL, fr. *Mola*, type genus + *-idae*] : a family of large pelagic marine fishes (order Plectognathi) that have very large heads, short compact bodies, and teeth fused to form a beak and that lack a dorsal fin — see MOLA

mo·li·men \mə'līmən\ *n, pl* **mo·lim·i·na** \-limənə\ [NL, fr. L, exertion, fr. *moliri* to struggle, fr. *moles* mass, burden — more at MOLE (structure)] : discomfort or sensations of tension preceding or accompanying menstruation

molminous *adj* [L *molimin-, molimen* + E *-ous*] *obs* : CUMBERSOME, WEIGHTY

mol·i·nary \'mäləˌnerē, 'mōl-\ *adj* [LL *molina* mill + E *-ary* — more at MILL] : of or relating to a mill or the process of grinding

mo·line \'mōlən, mō'līn\ *adj* [fr. (assumed) AF *moliné*, fr. OF *molin* mill, fr. LL *molinum* — more at MILL] *of a cross* : having the end of each arm forked and recurved — compare ANCRÉE, CROSS MOLINE, FOURCHÉE, PATY, RECERCELÉE; see CROSS illustration

molinet *n* -S [F *moulinet*, fr. MF *molinet*, dim. of *molin* mill] **1** *obs* : a stick for whipping chocolate **2** *obs* : a small grinding mill

moling *pres part of* MOLE

mo·lin·ia \mə'linēə\ *n, cap* [NL, fr. Juan Ignacio *Molina* †1829, Chilean naturalist + NL *-ia*] : a small genus of Eurasian grasses having narrow flat leaves, slender panicles, and awnless glumes — see MOOR GRASS 2

¹mo·li·nism \'mōləˌnizəm, 'mäl-\ *n* -S *usu cap* [Sp *molinismo*, fr. Luis *Molina* †1600 Span. Jesuit and theologian + Sp *-ismo* -ism] : a doctrine that it is man's free cooperation which makes it possible for him to perform a good act with God's helping grace — compare CONGRUISM, THOMISM

²molinism \"\ *n* -S *usu cap* [Sp *molinismo*, fr. Miguel de *Molinos* †*ab*1697 Span. priest and mystic + Sp *-ismo* -ism] : QUIETISM

¹mo·li·nist \-ˌnəst\ *n* -S *usu cap* [Sp *molinista*, fr. Luis *Molina* †1600 + Sp *-ista* -ist] : an advocate or follower of the doctrine of Luis Molina

²molinist \"\ *n* -S *usu cap* [Sp *molinista*, fr. Miguel de *Molinos* + Sp *-ista* -ist] : an advocate or follower of the quietism of Miguel de Molinos

mo·lisch reaction \'mōlish-\ *or* **molisch test** *n, usu cap M* [after Hans *Molisch* †1937 Ger. botanist] : a test for carbohydrate in which a reddish violet color is formed by reaction with alpha-naphthol in the presence of concentrated sulfuric acid

¹moll \'mȯl\ *adj* [G, fr. ML (*b*) *molle* b flat; fr. *b* + L *molle*, neut. of *mollis* soft, weak — more at MELT] : composed in the minor mode : MINOR ⟨G ~⟩

²moll \'mäl, 'mȯl\ *n* -S [prob. fr. *Moll*, nickname for *Mary*] **1** : PROSTITUTE **2 a** : DOLL 2 ⟨a sailor and his ~⟩ **b** : a gangster's girl friend — called also *gun moll* ⟨frequented by gangsters and their ~s —W.S.Maugham⟩

mollah *var of* MULLAH

moll-buzzer \'ˌ=ˌ=\ *n* [²*moll*] *slang* : a pickpocket whose victims are women

mo·lle \'mȯ(ˌ)yā\ *n* -S [AmerSp, fr. Quechua *mulli*] : PEPPER TREE 1

mollemock *var of* MALLEMUCK

mol·li·crush \'mäliˌkrüsh, -rəsh\ *vt* [perh. fr. E dial. *mully* powdery (fr. E ¹*mull* + *-y*) + E *crush*] *dial Eng* : to beat to jelly : CRUSH, PULVERIZE

¹mollie *var of* MOLLY

²mol·lie *also* **mol·ly** \'mälē\ *n, pl* **mollies** [by shortening] : MOLLIENISIA 2

mol·li·e·nis·ia \ˌmälēə'nisēə\ *n* [NL, irreg. after Comte François N. *Mollien* †1850 Fr. statesman] **1** *cap* : a genus of brightly colored topminnows of the family Poeciliidae highly valued as aquarium fishes — see SAILFIN **2** -S : any fish of the genus *Mollienisia*

mol·lier diagram \'mȯl(ˌ)yā-\ *or* **mollier chart** *n, usu cap M* [after Richard *Mollier* †1935 Ger. mechanical engineer] : a diagram showing thermodynamic properties of a substance with various quantities (as temperature and pressure) constant esp. in terms of entropy and enthalpy as coordinates

mol·li·fi·ca·tion \ˌmäləfə'kāshən\ *n* -S [ME *mollificacioun*, fr. MF *mollification*, fr. ML *mollification-, mollificatio*, fr. LL *mollificatus* (past part. of *mollificare* to soften) + *-ion-*, *-io* -ion — more at MOLLIFY] **1** : an act or instance of tempering : AMELIORATION, APPEASEMENT **2** : the quality or state of being mollified

mollifier *n* -S : one that mollifies ⟨vinegar . . . is itself a prime corrector and ~ —Thomas Fuller⟩

mol·li·fy \'mäləˌfī\ *vb* -ED/-ING/-ES [ME *mollefien, mollifien*; fr. MF *mollifier*, fr. LL *mollificare*, fr. L *mollis* soft + *-ficare* -fy — more at MELT] *vt* **1** : to soothe in temper or disposition : CONCILIATE, PACIFY ⟨*mollified* by her flattery⟩ ⟨should have *mollified* their artistic critics —Hunter Mead⟩ ⟨eager to ~ his own . . . nationalists —Claire Sterling⟩ **2** : to reduce the stiffness or rigidity of : SOFTEN ⟨shaving cream *mollifies* the beard⟩ ⟨they have riddled and *mollified* the rocks —D.C. Peattie⟩ ⟨plump cushions with bright covers ~ the lounges —Blanche E. Baughan⟩ **3 a** : to reduce in intensity or violence : ASSUAGE, AMELIORATE ⟨their solicitude *mollifies* his pique⟩ ⟨the behavior was not only *mollified* but improvement continued to recovery —*Diseases of the Nervous System*⟩ **b** : to make more agreeable : TEMPER ⟨prevailed on him to ~ his demands⟩ ⟨nor can the social necessity for the product ~ the process —Lewis Mumford⟩ ~ *vi, archaic* : to become less angry or obstinate : SOFTEN, RELENT ⟨the father *mollifies* and is reconciled to the marriage —*Examiner*⟩ **syn** see PACIFY

mol·li·fy·ing·ly *adv* : in a mollifying manner

mol·li·grant \'mäliˌgrant\ *n* -S [origin unknown] *Scot* : a wailing lamentation : COMPLAINT

mol·lis·i·a·ce·ae \məˌlisē'āsēˌē\ *n pl* [NL, fr. *Mollisia*, type genus (irreg. fr. L *mollis* soft + NL *-ia*) + *-aceae*] : a family of fungi (order Helotiales having the hymenium of the apothecium surrounded by a pseudoparenchymatous rim of dark mostly thick-walled cells

mol·lis·i·ose \mə'lisēˌōs\ *n* -S [NL *Mollisia* + E *-ose*] : LEAF SCORCH b

mol·li·sol \'mäləˌsäl\ *n* -S [L *mollis* soft + *solum* ground — more at MELT, SOIL] : the surface layer of permanently frozen ground in which the ice melts during the summer

mol·lu·go \mə'lü(ˌ)gō\ *n, cap* [NL, fr. L, stickseed, fr. *mollis* soft] : a genus of low chiefly tropical American herbs (family Aizoaceae) having whorled leaves and pedicellate flowers — see CARPETWEED

mol·lus·ca \mə'ləskə\ *n pl, cap* [NL, fr. L, neut. pl. of *molluscus* soft, fr. *mollis* — more at MELT] : a large phylum of invertebrate animals that include the chitons, tooth shells, snails, mussels and other bivalves, octopuses, and related forms and that have a soft unsegmented body lacking segmented appendages and commonly protected by a calcareous shell secreted by a mantle which extends from the body wall usu. as an enveloping fold; a muscular foot which is formed from part of the ventral surface of the body and is variously modified for creeping, digging, or swimming; a well-developed heart and vascular system and usu. one or more pairs of gills; a complex nervous system with several pairs of ganglia and longitudinal and transverse commissures; and frequently more or less complex eyes and otocysts — compare AMPHINEURA, CEPHALOPODA, GASTROPODA, LAMELLIBRANCHIA, SCAPHOPODA

mol·lus·can *also* **mol·lus·kan** \-kən\ *adj* [NL *Mollusca* + E *-an*] : of or relating to the Mollusca

mol·lus·ci·ci·dal \məˌləs(k)əˈsīdᵊl\ *also* **mol·lus·ca·ci·dal** \-skəˈ-\ *adj* : of, relating to, or being a molluscicide ⟨~ action⟩

mol·lus·ci·cide \məˈləs(k)əˌsīd\ *or* **mol·lus·ca·cide** \-skəˌ-\ *n* -S [*molluscicide* fr. NL *Mollusca* + E *-i-* + *-cide*; *molluscacide* fr. NL *Mollusca* + E *-cide*] : an agent for destroying mollusks (as snails)

mol·lus·civ·o·rous \ˌmäləˈs(k)iv(ə)rəs\ *adj* [NL *Mollusca* + E *-i-* + *-vorous*] : feeding upon mollusks

¹mol·lus·coid \məˈləˌskȯid\ *also* **mol·lus·coi·dal** \ˌmäləˈskȯidᵊl\ *adj* [*molluscoid* fr. NL *Molluscoidea*; *molluscoidal* fr. NL *Molluscoidea* + E *-al*] : of, like, or relating to the Molluscoidea

²molluscoid \"\ *n* -S : one of the Molluscoidea

mol·lus·coi·da \ˌmäləˈskȯidə\ [NL, fr. *Mollusca* + *-oida*] *syn of* MOLLUSCOIDEA

mol·lus·coi·dea \-dēə\ *n pl, cap* [NL, fr. *Mollusca* + *-oidea*] *in some classifications* : a phylum of invertebrate animals distinguished by possession of a lophophore and typically including the present groups Brachiopoda, Bryozoa, Entoprocta, and Phoronidea — **mol·lus·coi·de·an** \ˌ=ˈskȯidēən\ *adj or n*

¹mol·lus·cous \məˈləskəs\ *adj* [NL *Mollusca* + E *-ous*] : MOLLUSCAN

²molluscous \"\ *adj* [NL *molluscum* + E *-ous*] : of, relating to, or having the properties of a molluscum

mol·lus·cum \məˈləskəm\ *n, pl* **mollus·ca** \-kə\ [NL, fr. L *molluscum*, a fungus, fr. neut. of *molluscus* soft — more at MOLLUSCA] : any of several skin diseases marked by soft pulpy nodules — see MOLLUSCUM CONTAGIOSUM

molluscum con·ta·gi·o·sum \-kənˌtājē'ōsəm\ *n, pl* **mollusca contagio·sa** \-sə\ [NL, lit., contagious molluscum] : a mild chronic viral disease of the skin characterized by the formation of small nodules with a central opening and contents resembling curd

mol·lusk *or* **mol·lusc** \'mäləsk\ *n* -S [F *mollusque*, fr. NL *Mollusca*] : one of the Mollusca : SHELLFISH

moll-wei·de projection \'mȯlˌvīdə-\ *n, usu cap M* [after Karl B. *Mollweide* †1825 Ger. mathematician and astronomer] : an equal-area map projection capable of showing the entire surface of the earth in the form of an ellipse with all parallels as straight lines more widely spaced at the equator than at the poles, with the central meridian as one half the length of the equator, and with all other meridians ellipses equally spaced

¹mol·ly *or* **mol·lie** \'mälē, -li\ *n, pl* **mollies** [fr. *Molly, Mollie*, nickname for *Mary*] **1** *slang* : ²MOLL **2** *slang* : MOLLYCODDLE

²molly *or* **mollie** \"\ *n, pl* **mollies** [by shortening and alter.] : MALLEMUCK

³molly *var of* MALI

⁴molly *var of* MOLLIE

¹mollycoddle \'ˌ=ˌ=\ *n* [¹*molly* + *coddle*] **1** : a pampered darling : a spineless weakling ⟨his mother might turn him into a ~ —Aldous Huxley⟩ ⟨catch those ~s getting away from the steam heaters —*Everybody's Mag.*⟩; *specif* : an effeminate man ⟨the men . . . were ~s, and the women were sexually unemployed —Francis Hackett⟩ **2** : GOODY-GOODY ⟨these are the words not of a ~ or a sentimentalist, but of a veteran soldier —*Nation*⟩

²mollycoddle \"\ *vt* : to treat with fond indulgence : protect and cater to : PAMPER, SPOIL ⟨believes we have *mollycoddled* women too much —*N. Y. Times*⟩ ⟨judges ~ these young hoods —James McGlincy⟩ **syn** see INDULGE

mol·ly·cod·dler \'ˌ=ˌkäd(ᵊ)lə(r)\ *n* : one that mollycoddles

mol·ly·cot \'mäliˌkät\ *n* [¹*molly* + obs. *cot* man who does women's work, short for *cotquean*] *dial Eng* : one unduly concerned with housekeeping; *esp* : a man who takes an interest in or does housework usu. performed by women

mol·ly·grubs \'mäliˌgrəbz\ *var of* MULLIGRUBS

mol·ly·hawk \'mälēˌhȯk\ *n* -S [by folk etymology fr. *mallemuck*] : MALLEMUCK

mollymawk *var of* MALLEMUCK

mol·man \'mälmən\ *n, pl* **molmen** [ME, fr. *mol-* (fr. OE *māl* terms, agreement, pay) + *man* — more at MAIL] : one of a class of tenants in feudal England released from most of their service on condition of paying certain rents for their land

mo·loch \'mäläk, 'mōˌläk\ *n* [LL, an ancient Semitic deity, fr. Gk, fr. Heb *Mōlekh*] **1** -S *usu cap* : a tyrannical power to be propitiated by human subservience or sacrifice ⟨duty has become the *Moloch* of modern life —Norman Douglas⟩ ⟨began . . . to suspend members of his staff as a human sacrifice to propitiate the *Moloch* of

moloch 2b

POWER OF ATTORNEY

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Ish -Horowicz et al.	Confirmation No.:	8177
Serial No.:	09/783,931	Art Unit:	1646
Filed:	February 15, 2001	Examiner:	Claire M. Kaufman
For:	ANTIBODIES TO VERTEBRATE DELTA PROTEINS AND FRAGMENTS	Attorney Docket No.:	7326-122

REVOCATION AND POWER OF ATTORNEY

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Imperial Cancer Research Technology, Ltd. (assignee) hereby revokes any and all previous powers and appoints:

☒ Practitioners at Customer Number 20583

as his/her/its/their attorney(s) or agent(s) to prosecute the application identified above, and to transact all business in the United States Patent and Trademark Office connected therewith.

Please direct all correspondence address for the above-identified application to:

☒ The above mentioned Customer Number.

☒ Firm or Individual Name:

Address: Jones Day, 222 East 41st Street, New York, New York 10017
Telephone: (212) 901-9028

Statement Under 37 C.F.R. 3.73(b)

Imperial Cancer Research Technology, Ltd. states that it is:

☒ the co-assignee with Yale University, and that Imperial Cancer Research Technology, Ltd. and Yale University together own the entire right, title, and interest; or

☐ an assignee of less than the entire right, title and interest.
The extent (by, percentage) of its ownership interest is %

in the patent application/patent identified above by virtue of either:

☒ An assignment from inventors David Ish-Horowicz, Domingos M.P. Henrique and Julian Hart Lewis to Imperial Cancer Research Technology, Ltd. of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office on June 8, 1998 at Reel 9250 , Frame 0339.

OR

☐ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as shown below:

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The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

ASSIGNEE: Imperial Cancer Research Technology, Ltd.

Date: 8.9.2004 Signature: Carola Lempke

Typed Name: CAROLA LEMPKE

Position/Title: IP Manager – ICRT

Note: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required.

☒ Total of 2 forms are submitted.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Ish-Horowicz *et al.*	Confirmation No.: 8177
Application No.: 09/783,931	Group Art Unit: 1646
Filed: February 15, 2001	Examiner: Claire M. Kaufman
For: ANTIBODIES TO VERTEBRATE DELTA PROTEINS AND FRAGMENTS	Attorney Docket No.: 7326-122

DECLARATION OF DRS. DOMINGOS M.P. HENRIQUE, JULIAN H. LEWIS, DAVID ISH-HOROWICZ, SPYRIDON ARTAVANIS-TSAKONAS, AND GRACE E. GRAY UNDER 37 C.F.R. 1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

We, DOMINGOS M.P. HENRIQUE, JULIAN H. LEWIS, DAVID ISH-HOROWICZ, SPYRIDON ARTAVANIS-TSAKONAS, and GRACE E. GRAY hereby state and declare as follows:

1. Domingos M.P. Henrique is a citizen of Portugal residing at Av Prof Egas Moniz, 1649-028 Lisboa, Portugal. Julian H. Lewis is a citizen of the United Kingdom residing at 60 Sandfield Road, Headington, Oxford OX3 7RJ, United Kingdom. David Ish-Horowicz is a citizen of the United Kingdom residing at 2 Lower Fisher Row, Oxford, OX1 1JY, United Kingdom. Spyridon Artavanis-Tsakonas is a citizen of the United States of America residing at 167 Willard Road, Brookline, Massachusetts 02445. Grace E. Gray is a citizen of the United States of America residing at 6505 Stoneham Road, Bethesda, Maryland 20817.

2. We are the inventors of the subject matter described and claimed in the above-identified patent application.

3. Drs. Domingos M.P. Henrique, Julian H. Lewis and David Ish-Horowicz are co-authors of the publication entitled "Expression of a Delta homologue in prospective neurons in the chick" (hereinafter "Henrique *et al.*"), Nature, 1995, 375:787-790.

4. The contributions of the other co-authors of Henrique *et al.*, Julie Adam, Anna Myat and Ajay Chitnis to the work described in Henrique *et al.* were as follows: Julie Adam performed the preparation of chick embryos for the expression studies and participated in the confocal analysis of bromodeoxyuridine-labeled embryos. Anna Myat performed the preparation of chick embryos for the expression studies and assisted with the sequencing of the original PCR amplification product from the chick Delta gene cloned by Dr. Domingos M.P. Henrique. Ajay Chitnis performed the isolation of the full-length cDNA of *Xenopus* Delta using a fragment of the gene cloned by Dr. Domingos M.P. Henrique and determined the sequence of the full-length *Xenopus* Delta cDNA. These individuals worked under the direction of Drs. Domingos M.P. Henrique, Julian H. Lewis and/or David Ish-Horowicz and, while co-authors of Henrique *et al.*, are not co-inventors of the subject matter that is described and claimed in the above-identified patent application.

5. We declare further that all statements made in this Declaration of our own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

8 September 2004
DATE

DOMINGOS M.P. HENRIQUE

DATE

JULIAN H. LEWIS

DATE

DAVID ISH-HOROWICZ

DATE

SPYRIDON ARTAVANIS-TSAKONAS

DATE

GRACE E. GRAY

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Ish-Horowicz *et al.* **Confirmation No.:** 8177

Application No.: 09/783,931 **Group Art Unit:** 1646

Filed: February 15, 2001 **Examiner:** Claire M. Kaufman

For: ANTIBODIES TO VERTEBRATE DELTA PROTEINS AND FRAGMENTS **Attorney Docket No.:** 7326-122

DECLARATION OF DRS. DOMINGOS M.P. HENRIQUE, JULIAN H. LEWIS, DAVID ISH-HOROWICZ, SPYRIDON ARTAVANIS-TSAKONAS, AND GRACE E. GRAY UNDER 37 C.F.R. 1.132

Mail Stop Amendment
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2. We are the inventors of the subject matter described and claimed in the above-identified patent application.

3. Drs. Domingos M.P. Henrique, Julian H. Lewis and David Ish-Horowicz are co-authors of the publication entitled "Expression of a Delta homologue in prospective neurons in the chick" (hereinafter "Henrique *et al.*"), Nature, 1995, 375:787-790.

4. The contributions of the other co-authors of Henrique *et al.*, Julie Adam, Anna Myat and Ajay Chitnis to the work described in Henrique *et al.* were as follows: Julie Adam performed the preparation of chick embryos for the expression studies and participated in the confocal analysis of bromodeoxyuridine-labeled embryos. Anna Myat performed the preparation of chick embryos for the expression studies and assisted with the sequencing of the original PCR amplification product from the chick Delta gene cloned by Dr. Domingos M.P. Henrique. Ajay Chitnis performed the isolation of the full-length cDNA of *Xenopus* Delta using a fragment of the gene cloned by Dr. Domingos M.P. Henrique and determined the sequence of the full-length *Xenopus* Delta cDNA. These individuals worked under the direction of Drs. Domingos M.P. Henrique, Julian H. Lewis and/or David Ish-Horowicz and, while co-authors of Henrique *et al.*, are not co-inventors of the subject matter that is described and claimed in the above-identified patent application.

5. We declare further that all statements made in this Declaration of our own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

_____ _____

DATE DOMINGOS M.P. HENRIQUE

8 September 2004

8/9/04
DATE

JULIAN H. LEWIS

8/9/04
DATE

DAVID ISH-HOROWICZ

DATE

SPYRIDON ARTAVANIS-TSAKONAS

DATE

GRACE E. GRAY

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Ish-Horowicz *et al.* **Confirmation No.:** 8177

Application No.: 09/783,931 **Group Art Unit:** 1646

Filed: February 15, 2001 **Examiner:** Claire M. Kaufman

For: ANTIBODIES TO VERTEBRATE DELTA PROTEINS AND FRAGMENTS **Attorney Docket No.:** 7326-122

DECLARATION OF DRS. DOMINGOS M.P. HENRIQUE, JULIAN H. LEWIS, DAVID ISH-HOROWICZ, SPYRIDON ARTAVANIS-TSAKONAS, AND GRACE E. GRAY UNDER 37 C.F.R. 1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

We, DOMINGOS M.P. HENRIQUE, JULIAN H. LEWIS, DAVID ISH-HOROWICZ, SPYRIDON ARTAVANIS-TSAKONAS, and GRACE E. GRAY hereby state and declare as follows:

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DATE DOMINGOS M.P. HENRIQUE

DATE — JULIAN H. LEWIS

DATE — DAVID ISH-HOROWICZ

9/8/2004
DATE — SPYRIDON ARTAVANIS-TSAKONAS

DATE — GRACE E. GRAY

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Ish-Horowicz *et al.*	**Confirmation No.:** 8177
Application No.: 09/783,931	**Group Art Unit:** 1646
Filed: February 15, 2001	**Examiner:** Claire M. Kaufman
For: ANTIBODIES TO VERTEBRATE DELTA PROTEINS AND FRAGMENTS	**Attorney Docket No.:** 7326-122

DECLARATION OF DRS. DOMINGOS M.P. HENRIQUE, JULIAN H. LEWIS, DAVID ISH-HOROWICZ, SPYRIDON ARTAVANIS-TSAKONAS, AND GRACE E. GRAY UNDER 37 C.F.R. 1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
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